UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,829	01/31/2006	Chikara Jin	TOYA145.001APC	7514

20995 7590 01/25/2010

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
01/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/566,829	JIN ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendments filed 9/29/2009 were entered.

Response to Arguments

2. Applicants' arguments, filed 9/29/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. **Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Ninomiya et al* (cited in a previous Action) in view of *Friedman et al* (cited in a previous**

Action), *Nguyen et al* (cited in a previous Action), *David et al* (cited in a previous Action), *Bowen et al* (cited in a previous Action), and *Quercia et al* (cited in a previous Action).

6. As discussed in the previous Action mailed on 5/29/2009, Instant claim 1 is drawn to a medicine for oral administration comprising a jellied pharmaceutical composition for oral administration wherein the composition comprises granisetron hydrochloride, a carrageenan (specifically kappa (κ)-carrageenan and/or iota (ι)-carrageenan), locust bean gum, sodium polyacrylate, D-sorbitol, glycerin, and water, wherein the composition has a pH of 7 or less.

7. **The following is a reiteration of the rejection presented in the previous Action mailed on 5/29/2009**:

8. *Ninomiya et al* teach medicines for oral administration comprising a jellied pharmaceutical composition (Abstract) and which "easily taken by patients of advanced age or patients with dysphagia" (Column 1, Lines 3-4). More specifically, *Ninomiya et al* disclose seven embodiments wherein the composition comprises κ-carrageenan, locust bean gum, sodium polyacrylate, D-sorbitol and water (Columns 10-12, Examples 1-7, Tables 1-5). However, *Ninomiya et al* do not teach compositions comprising **(1)** granisetron HCl, **(2)** glycerin and **(3)** wherein the pH of the composition is 7 or less.

9. **As to (1):** it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to include granisetron HCl in the jellied pharmaceutical composition taught by *Ninomiya et al*. Although *Ninomiya et al* specifically disclose compositions wherein the medically active ingredient is domperidone (Column 10, Examples 1-2, Table 1), acyclovir (Columns 10-11, Examples 3-4, Table 2), sodium loxoprofen (Column 11, Example 4, Table 3), famatodine (Columns 11-12, Example 6, Table 4) or terfenadin (Column

12, Example 7, Table 5), they also specifically teach that "**any** medically effective components can be used, without particularly being limited" (Column 5, Lines 16-17, emphasis added). Accordingly, the skilled artisan would not have considered the teaching of *Ninomiya et al* to be limited to jellied pharmaceutical compositions comprising only domperidone, sodium loxoprofen, famatodine, or terfenadin, and would have found it *prima facie* obvious to substitute (in place of domperidone, sodium loxoprofen, famatodine, and terfenadin) **any** medically effective ingredient. Moreover, the person of ordinary skill in the art would have found it *prima facie* obvious to use granisetron HCl, specifically, as the medically effective ingredient in the composition taught by *Ninomiya et al*. As evidenced by *Friedman et al*, "5-HT3-receptor antagonists have become the standard of care for the prevention of acute nausea and vomiting associated with chemotherapy. Granisetron (KYTRIL®, SmithKline Beecham Pharmaceuticals, Philadelphia PA) is effective in preventing nausea and vomiting induced by emetogenic chemotherapy" (Page 137, Column 1). Significantly, KYTRIL® (as taught by *Friedman et al* for the treatment of emesis during chemotherapy) is the hydrochloride salt of granisetron. And, as taught by *Nguyen et al*, "[d]ysphagia is a common, debilitating and potentially life-threatening sequela of concurrent chemoradiation for head and neck malignancy" (Abstract). Accordingly, in view of *Ninomiya et al* which, as discussed above, teach that the jellied pharmaceutical composition is "easily taken by patients of advanced age or patients with dysphagia" (Column 1, Lines 3-4) the skilled artisan would have been motivated to provide granisetron HCl (for the treatment of nausea during chemotherapy) in a form which can be easily taken by pateints having dysphagia. Accordingly, it would have been *prima facie* obvious to a person of ordinary skill in

the art at the time the invention was made to use granisetron HCl in the jellied pharmaceutical composition taught by *Ninomiya et al* with a reasonable expectation of success.

10. **As to (2):** it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to include glycerin in the jellied pharmaceutical composition taught by *Ninomiya et al*. As evidenced by *David et al* (available online at http://www.chem.yorku.ca/hall_of_fame/essays96/glycerol.htm as of April 20, 2001 based on the attached Internet Archive Report), "[a]s a humectant, glycerol constitutes an important pharmaceutical ingredient to prevent the drying out of preparations, particularly ointments and creams" (Paragraph 4). Indeed, *Bowen et al* teach oral gel compositions which may comprise humectants, including glycerin, "in an amount of about 5 to about 90 weight percent, more typically about 10 to about 60 weight percent" (Paragraph 0033). Accordingly, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to include glycerin in the jellied pharmaceutical composition taught by *Ninomiya et al*. The skilled artisan would have been motivated to do so in view of *David et al*, in order to prevent the drying out of the jellied preparation taught by *Ninomiya et al* with a reasonable expectation of success. Furthermore, in view of *Bowen et al*, the concentration of glycerin recited by instant claim 9 is also *prima facie* obvious. As stated by MPEP 2144.05, "[i]n the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art'" a *prima facie* case of obviousness exists (quoting *In re Wertheim*, 541 F.2d 257 (CCPA 1976)). Thus, since the claimed ranges recited by instant claim 9 lie inside ranges disclosed by the prior art, they are *prima facie* obvious.

11. **And as to (3):** it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to maintain the pH of the composition to pH 7 or below. Although *Ninomiya et al* do not specifically teach a composition wherein the pH is 7 or less (instead, teaching only that the compositions "retain preservation stability at the medical level in terms of maintenance of appearance and pH" Column 14, Line 67 to Column 15, Line 1), it is well known in the art that the pH of a pharmaceutical composition can influence drug stability, storage and preservation. In particular, *Quercia et al* teach that granisetron HCl in oral liquid formulation is stable in the pH range from 2.7 to 2.8 (Abstract and Page 1406, Column 1, Results Section). Thus it would have been prima facie obvious to a person of ordinary skill in the art to formulate the composition taught by *Ninomiya et al* having a pH of 7 or less. In view of *Quercia et al*, the skilled artisan would have found it *prima facie* obvious to formulate the composition comprising granisetron HCl at a pH of 7 or below in order to provide a compositions which retain stability with a reasonable expectation of success.

12. Accordingly, in view of all of the foregoing reasons, instant claims 1 and 9 are rejected as *prima facie* obvious.

13. **Response to Applicants' Arguments**:

14. Applicants acknowledge that *Ninomiya et al* teach compositions comprising k-carrageenan, locust bean gum, sodium polyacrylate, D-sorbitol, and water. However, they do not teach granisetron HCl, glycerin and where the pH is 7 or less. As to the inclusion of granisetron HCl, Applicants further note that "were they to combine Granisetron HCl with the other components taught by this reference, they would have encountered the foaming problem" (Applicant Argument, Pages 2-3). That is, "Granisetron HCl has a tendency to foam when

blended with carrageenan, locust bean gum and sodium polyacrylate." (Applicant Argument, Page 2; see also Declaration, Page 1, Item 3). Although Applicants do not explicitly state the following, it is possible that Applicants are intending to argue that the skilled artisan would **not** have considered including Granisetron HCl in the composition taught by *Ninomiya et al* because the skilled artisan, at the time the invention was made, would have recognized that the inclusion of Granisetron HCl to the composition would result in foaming, thereby rendering the resulting jellied pharmaceutical composition ***unusable or inoperable***. If so, Applicants should clearly indicate that this is being argued since "[t]he test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference… Rather, the test is what the combined teachings of those references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413 (CCPA 1981). Or, as stated in *In re Sneed*, 710 F.2d 1544 (Fed. Cir. 1983), "it is not necessary that the inventions of the references by physically combinable to render obvious the invention under review." In the instant case, as discussed above, the combined teachings motivate the inclusion of Granisetron HCl into the jellied pharmaceutical composition taught by *Ninomiya et al* for the reasons discussed above. As such, the inclusion of Granisetron HCl in the jellied pharmaceutical composition taught by *Ninomiya et al* is *prima facie* obvious even if the elements are not physically combinable. However, the claimed combination cannot change the principle of operation of the primary reference or render the reference inoperable for its intended purpose. Since Applicants have not indicated that the foaming problem would render the composition of *Ninomiya et al* unsatisfactory for its intended purpose (i.e., the "foaming problem" would render the jellied pharmaceutical composition inoperable for the administration of the pharmaceutical),

Applicants' arguments are not considered persuasive. **Furthermore**, since "[u]pon inclusion of D-sorbitol and glycerin in a composition comprising granisetron HCl, the specified carrageenans, locust bean gum and sodium polyacrylate, the foaming problem is resolved without adversely affecting the appearance of the final product" (Applicant Argument, Page 2), the skilled artisan (formulating the *prima facie* obvious composition discussed above, which ***would*** include glycerin as a humectant) would not have encountered any foaming problem while making the *prima facie* obvious composition and, thus, would not have resulted in an inoperable product. As to the obviousness of including glycerin in the composition, Applicants first argue that "one of ordinary skill in the art faced with the foaming problem... would not turn to glycerin to solve the foaming problem" (Applicant Argument, Page 3). However, it is not necessary that the prior art suggest the combination of references to achieve the ***same*** advantage or result discovered by Applicant (in this case, to solve the foaming problem). Rather, the reason or motivation to modify a reference to arrive at the claimed invention can be for a different purpose or to solve a different problem (in this case, to provide a humectant). The fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability with the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58 (Bd. Pat. App. & Inter. 1985). Second, Applicants argue that "there would be no apparent reason to add an additional humectant as the composition already necessarily includes sorbitol which is an effective humectant" (Applicant Argument, Page 4). However, in response to Applicants' assertion, it is noted that the inclusion of more than one humectant in a single composition is not uncommon in the art. For example, *Barel et al* (Handbook of Cosmetic Science and Technology, 2001), discussing personal care products,

teach that "[t]he primary used humectant in personal care products is glycerin; it tends to provide heavy and tacky feel which can be overcome by using it in combination with other humectants such as sorbitol" (Page 406). Thus, Applicants' argument that there would be no apparent reason to add an additional humectant is not considered persuasive. That is, it is not uncommon to include multiple humectants such as, for example, glycerin and sorbitol in combination, in a single composition in view of *Barel et al*.

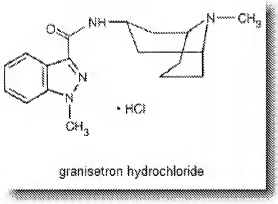
15. Accordingly, the rejection of claims 1 and 9 as *prima facie* obvious is maintained.

16. Since Applicants do not traverse the rejection of claim 2 beyond that which is already discussed above and considered not persuasive, the rejection of claim 2 (which is reiterated as follows) is also maintained:

17. **Claim 2 is maintained rejected under 35 U.S.C. 103(a) as being unpatentable over *Ninomiya et al* (cited in a previous Action) in view of *Friedman et al* (cited in a previous Action), *Nguyen et al* (cited in a previous Action), *David et al* (cited in a previous Action), *Bowen et al* (cited in a previous Action), and *Quercia et al* (cited in a previous Action) as applied to instant claim 1 above, in further view of *Hai* (cited in a previous Action) and *Shushin et al* (cited in a previous Action).**

18. Additionally, the composition of *Ninomiya et al* does not teach the inclusion of a reductant as recited by instant claim 2. As discussed in a previous Action, *Hai* teaches that "[t]he desirability of providing pharmaceutical formulations in which an oxidation-susceptible active drug ingredient or ingredients are protected against oxidative degradation inherent to prolonged storage is a concept well known to, and appreciated by, one of ordinary skill in the art. Anti-oxidants commonly employed in various pharmaceutical formulations may include, inter

alia, vitamin E, ascorbic acid, BHT (butylated hydroxytoluene), BHA (butylated hydroxyanisole), and the like." In the instant case, granisetron HCl is oxidation-susceptible. Specifically, granisetron HCl, which is represented as having the following structure



granisetron hydrochloride

encompasses an amide which one of ordinary skill in the art would recognize as susceptible to oxidation in view of *Shushin et al*, which specifically discuss oxidation of amide compounds. Since developing pharmaceutical compositions capable of prolonged storage is desirable, it would have been *prima facie* obvious to a person of ordinary skill in the art to combine a reductant, as taught by *Hai*, with the composition taught by *Ninomiya et al*. As such, instant claim 2 is rejected as *prima facie* obvious.

Conclusion

No new ground(s) of rejection are presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1628

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642